"Laboratory Contributions to the Tobacco-Cancer Problem"
Dr. E.L. Wynder British Medical Journal, 2/5/59

also set out to test whether cigarettes smoked halfway or to the butt end would show different activity, since repyrolysis of condensed tar might produce more carcinogenic material. However, the results again showed a similarity in biological activity even though the tar yield of cigarettes smoked to the very butt end is obviously greater than of those smoked halfway down.[37]

Finally, we have studied the comparative activity of cigar, pipe, and cigarette tars. We found cigar and pipe tar somewhat more active, which, we believe, is due to the fact that cigar and particularly pipe tobacco burns at a high level for a longer period of time than does cigarette tobacco, even though the maximum temperature of cigarettes is higher than that of pipes. These temperature studies have been reported in detail by Touey and Mumpower, and are summarized in Fig 7.[24 43] In burning at a high temperature for a longer

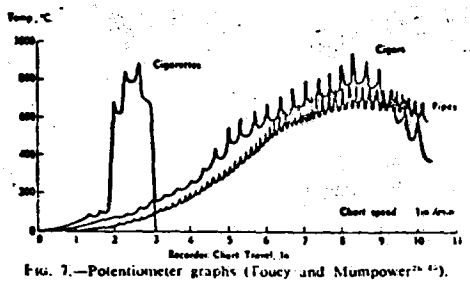

FIG. 7.—Potentiometer graphs (Touey and Mumpower[24 43]).

period of time the combustion may be more complete in cigars and pipes. Obviously the formation of the carcinogens from organic material is not only a consequence of maximum temperature, but also of the duration of contact with a given temperature level. Present evidence strongly suggests that modification of temperature levels, if achieved, could influence the formation of carcinogens in tobacco.

Study of Precursors

By studying precursors we planned to determine whether there were any components in tobacco smoke condensate which would be particularly susceptible to the formation of higher aromatic polycyclics. We washed tobacco with hot hexane and smoked the extracted tobacco. Of immediate interest is the fact that, though only 5.4% of the tobacco by weight was removed, the tar yield of this cigarette was 35% less than that of an ordinary cigarette.[31] However, on a gramme-to-gramme basis, one of the two experiments showed a somewhat decreased activity and the other showed no decrease in activity from regular tar. Therefore, at present we must conclude that this method cannot effectively reduce the carcinogenic activity of tobacco tar. Lindsey had previously shown some reduction in benzpyrene content of hexane-extracted tobacco.[14] However, our studies do not show a reduction of benzpyrene in hexane-extracted tars.

Lindsey has shown that a large variety of agents present in tobacco can produce higher aromatic polycyclics when pyrolysed.[12] Lam has pyrolysed some of the sterols present in tobacco and has identified higher aromatic polycyclics.[25] We have shown this pyrolysate to be biologically active on mouse skin.[32] In view of these observations it would be most difficult to remove any given substance from tobacco in the absence of which no polycyclics could be formed. We believe, therefore, that even though the different components in tobacco may vary in their relative susceptibility to form higher aromatic polycyclics, a removal of certain substances from the tobacco itself would not be a practical way of reducing its carcinogenic activity upon being smoked.

Practical Preventive Measures

The practical preventive measures as derived from completed laboratory work fall into the following categories.

1. *Lowering of Tar Content in View of Studies on Dose-Response Levels.*—This can be attained through effective filtration and tobacco selection. The greater the decrease in tar content of a given cigarette the lower the liability to cancer development. This is a practical step which can be undertaken by the tobacco industry without delay.

2. *Temperature Reductants.* — We are currently engaged in a study of a number of substances, including aluminium products, to determine whether the temperature of the tobacco during smoking can be lowered sufficiently to influence the formation of polynuclear substances.[33] A number of suggestions have been made to cool the main stream of the smoke. However, since the carcinogens undoubtedly are formed in the burning process, it is here that we must concentrate our efforts.

3. *Modification of Pyrolysis.*—Through the use of a variety of catalysts we are currently engaged in determining whether the polynuclear content of tobacco smoke condensate can be reduced.[34] The idea of catalysts, which is useful in the petroleum industry, may be less applicable in the case of tobacco because of shorter contact time. However, work completed so far suggests that the polynuclear content can be altered. It also seems to affect the proportion of different polynuclear substances. These studies are still in the preliminary stage, and it remains to be determined through combined biological and chemical investigations whether there is a particular catalyst or group of catalysts which could reduce in a practical fashion the carcinogenic activity of the tobacco smoke condensate.

Conclusion

In summary, we have reviewed the work being conducted in various laboratories throughout the world, and particularly in our own laboratory, relating to the tobacco cancer problem. We have stated the purpose of the laboratory experiment, the direction in which it must go, and have emphasized the relationship that it bears to the human epidemiological study. Like any other phase of scientific investigation, it is the co-operation in different areas of scientific activity which furthers the achievement of a solution to any given problem. While only the epidemiological study can give definite proof of the relationship of smoking and lung cancer, the studies in the laboratory are essential in providing a practical solution to this problem, short of abolishing the smoking habit. Knowing that man will continue to smoke regardless of the evidence, we must expand our laboratory work in order to provide a practical solution to the problem. The thousands of

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